REMARKS

Entry of the foregoing and reexamination and reconsideration of the subject application, as proposed to be amended, pursuant to and consistent with 37 C.F.R. §1.116, are respectfully requested in light of the following remarks.

STATUS OF CLAIMS AND AMENDMENTS

Claims 1, 9-11, 13, 14, 16, 17, 21, 24, 25, 27-29, 43-51 and 67-69 are now in this application. Claims 2-8, 12, 15, 18-20, 22, 23, 26, 30-42 and 52-60 were previously cancelled. Claims 61-66 were cancelled in this amendment.

Claims 1, 24, 25 and 27-29 have been amended to delete the recitation of the optional inclusion of at least one compound which stimulates the activity of aspartylglucosaminidase (AGA). Claim 13 has been amended to depend from claim 44 and to recite the composition comprising sodium dodecyl sulfate or sodium lauryl ether sulfate comprises from 0.01% to 50% sodium dodecyl sulfate or sodium lauryl ether sulfate by weight of the composition. Support for this amendment is found in the specification at least on page 11, paragraphs [0050-0051]. Claim 14 has been amended to recite the weight percentages as recited in amended claim 13. Claims 43-51 have been amended to recite that the regime or regimen further comprises topically applying onto the skin sodium dodecyl sulfate or sodium lauryl ether sulfate. Support for this amendment is found in the specification at least on page 13, paragraph [0069]. Claim 44 has been amended to recite that the sodium dodecyl sulfate or sodium lauryl ether sulfate is formulated into a topically applicable cosmetic/dermatological composition. Support for this amendment is found in the specification at least on page 13, paragraph [0060].

Claims 67-69 have been added. Claims 67 recited a regime or regimen as defined by Claim 44 wherein said composition comprising sodium dodecyl sulfate or sodium lauryl ether sulfate is applied together with said composition comprising aspartylglucosaminidase (AGA). Support for this amendment is found in the specification at least on page 13, paragraph [0060]. Claim 68 recites a regime or regimen as defined by Claim 44 wherein said composition comprising sodium dodecyl sulfate or sodium lauryl ether sulfate is applied separately from said composition comprising aspartylglucosaminidase (AGA). Support for this amendment is found in the specification at least on page 13, paragraph [0060]. Claim 69 recites a regime or regimen as defined by Claim 44 wherein said composition comprising sodium dodecyl sulfate or sodium lauryl ether sulfate is the same composition comprising aspartylglucosaminidase (AGA). Support for this amendment is found in the specification at least on page 13, paragraph [0060].

No new matter has been added in making these amendments.

CLAIM REJECTIONS - 35 U.S.C. § 112

1. Claims 1, 9-11, 13, 14, 16, 17, 21, 24, 25, 27-29, and 43-51 have been rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. Applicants submit that all of their claims are free of this rejection.

The Office Action indicates the claims recite "at least one compound which stimulates the activity of aspartylglucosamidase (AGA)" but the specification only indicates sodium dodecyl sulphate (SDS) and sodium lauryl sulfate, as suitable

compounds, and does not describe any other compounds appropriate for stimulating the activity of AGA.

Claims 1, 13, 14, 24, 25, 27-29, and 43-51 have been amended and no longer recite "at least one compound which stimulates the activity of aspartylglucosamidase (AGA)".

Applicants respectfully submit that this rejection is therefore rendered moot.

2. Claims 43-51 have been rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement. Claims 43-51 previously recited the at least one compound which stimulates the activity of AGA is sodium dodecyl sulfate (SDS) or sodium lauryl ether sulfate.

Claim 27 has been amended to delete the optional treatment with at least one compound which stimulates the activity of aspartylglucosaminidase (AGA). Amended Claims 43-51 have been amended and do not recite that the at least one compound which stimulates the activity of AGA is sodium dodecyl sulfate (SDS) or sodium lauryl ether sulfate.

Applicants note for the record that the specification clearly teaches that sodium dodecyl sulfate and sodium lauryl ether sulfate are activators of AGA. The Office Action notes that Enomaa et al. observes the effects of SDS on AGA activity at various temperatures and SDS concentrations. Enomaa et al. teaches that the denaturing of AGA in the presence of SDS occurs only at elevated temperatures. Note the following discussion of Figs. 2 and 3 found on page 615 of Enomaa et al.

> If the AGA protein was not denatured by boiling with SDS before application on SDS/PAGE in Western-blot analysis, these antibodies identified a high-molecular-mass AGA band representing the native form of all the

> enzyme with detectable enzymatic activity (Fig. 2). Boiling of the enzyme with 0.5% SDS before SDS/PAGE and after Western-blot analysis resulted in the disappearance of the high-molecular-mass band and appearance of four bands of molecular mass 17/18kDa and 24/25dKa (Fig. 2). Further studies of the effect of SDS on the native AGA enzyme revealed that only temperatures higher than 60°C resulted in the decrease of AGA activity in the presence of 0.1-0.5% SDS at pH 7 (Fig. 3), demonstrating the AGA protein's exceptional resistance to SDS at lower temperatures. (Emphasis added.)

The Office Action states:

> Figure 3 on page 614 of Enomaa et al. compares the activity of AGA in the absence or presence of SDS, and it is evident that for every temperature and concentration tested, the presence of SDS decreased the activity of AGA. (page 3-4 of Office Action)

Applicants note that Figure 3 of Enomaa et al. does not contain any information to allow one to determine what values and comparisons are statistically significant. Applicants respectfully submit that lacking such information it is improper to draw conclusions that specifically contradict the teachings by the author of the paper. Enomaa et al. state "Further studies of the effect of SDS on the native AGA enzyme revealed that only temperatures higher than 60°C resulted in the decrease of AGA activity in the presence of 0.1-0.5% SDS at pH 7 (Fig. 3), demonstrating the AGA protein's exceptional resistance to SDS at lower temperatures." (Emphasis added.) The conclusions in the Office Action contradicts the explicit teaching stated by Enomaa et al. The prior art does not teach anything contrary to the teachings of applicants' specification.

3. Claims 1, 9-11, 13, 14, 16, 17, 21, 24, 25, 27-29, and 43-51 have been rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicants submit that all of their claims are free of this rejection.

The Office Action indicates that claims 1, 24, 25 and 27-29 are indefinite since the use of the term "optionally" in the claim does not clearly indicate whether at least one compound which stimulates the activity of AGA is present and a critical element.

Amended Claims 1, 24, 25 and 27-29 do not recite "optionally" language.

Applicants respectfully submit that this rejection is therefore rendered moot.

CLAIM REJECTIONS - 35 U.S.C. § 103

Claims 1, 9-11, 13, 14, 16, 17, 21, 24, 25, 27-29, and 61-66 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over Fein (US 2003/0026794) in view of Baumann et al. (*Biochem. J.* 1989, 262:189-194.) Applicants submit that all of the claims now in this application are patentable over Fein alone or in view of Baumann et al.

The Office Action states that Fein differs from the claimed invention in that it does not teach that the hydrolase enzyme topically applied to the skin is aspartylglucosaminidase (AGA). Fein teaches the use of hydrolases belonging in EC classes 3.1 - 3.4, as well as nucleases, nucleosidases and nucleoside phosphorylases. (See page 4, paragraph [0044])

Baumann teaches that human aspartylglucosaminidase is in EC class 3.5.1.26. (See abstract)

The Office Action states:

> At the time the invention was made, it would have been obvious to the person of ordinary skill in the art to have used aspartylglucosaminidase as the hydrolase enzyme of the Fein enzyme formulation for treating skin. One of ordinary skill in the art would have been motivates to do this since there would have been a reasonable expectation of success in substituting one hydrolase for another. Furthermore, Fein does not limit which hydrolases may be used in his invention." (see page 7)

Applicants respectfully submit that Fein does limit which hydrolases may be used in his invention. Claims must be read in light of the specification. Fein does not state that all hydrolases may be used, but rather indicates that hydrolases in classes 3.1 - 3.4, as well as nucleases, nucleosidases and nucleoside phosphorylases. (See page 4, paragraph [0044]). Fein states:

> "Although not included in the above classification [EC class 3.1-3.4], nucleases, such as deoxyribonuclease and ribonuclease, nucleosidases, and nucleoside phosphorylases are also encompasses by the invention." (information in brackets added by Applicants representative for clarity)

This statement by Fein makes it clear that fact Fein did not consider all hydrolases as being encompassed by his invention but only those in classes 3.1-3.4 and nucleases, nucleosidases, and nucleoside phosphorylases. If Fein had considered that all hydrolases were encompasses by the invention we would not have needed to specifically recite only those hydrolases in groups 3.1-3.4 and the few exceptions outside that group.

To establish a *prima facie* case of obviousness, three basic criteria must be met. (MPEP 2143) First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill

in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations.

To establish a *prima facie* case of obviousness, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. There is no suggestion or motivation in Fein to use aspartylglucosaminidase (AGA), a hydrolase that is not included within the vast group of hydrolases disclosed in his invention. Nor is there any suggestion or motivation in Baumann to use AGA in a regime or regimen to promoting desquamation of the skin and/or for promoting hydration of the skin. One of ordinary skill in the art, upon reading Fein, would not be motivated to try hydrolases outside of the specific groups cited by Fein for at least two reasons. First, one of ordinary skill in the art would recognize that there are a vast number of hydrolases in various other classification groups that are not encompassed by the specific group of hydrolases described by Fein and there is nothing to suggest trying a hydrolase in any of these non-included groups. Also, one of ordinary skill in the art would recognize that because Fein teaches the use of hydrolases in groups 3.1-3.4 and only nucleases, nucleosidases, and nucleoside phosphorylases outside of that group, there would be some reason why Fein did not list the other hydrolases not encompassed by his invention. Thus Fein teaches away from using other hydrolases. Therefore there is no suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings to obtain the Applicant's invention.

To establish a *prima facie* case of obviousness, there must be a reasonable expectation of success. There is no reasonable expectation of success in substituting one hydrolase for another. This can be seen by a quick evaluation of ester hydrolases, which classified as being in EC 3.1. The subgroups of ester hydrolases are shown below:

EC 3.1	Acting on ester bonds
EC 3.1.1	Carboxylic ester hydrolases
EC 3.1.2	Thioester hydrolases
EC 3.1.3	Phosphoric monoester hydrolases
EC 3.1.4	Phosphoric diester hydrolases
EC 3.1.5	Triphosphoric monoester hydrolases
EC 3.1.6	Sulfuric ester hydrolases
EC 3.1.7	Diphosphoric monoester hydrolases
EC 3.1.8	Phosphoric triester hydrolases
EC 3.1.11	Exodeoxyribonucleases producing 5'-phosphomonoesters
EC 3.1.13	Exoribonucleases producing 5'-phosphomonoesters
EC 3.1.14	Exoribonucleases producing 3'-phosphomonoesters
EC 3.1.15	Exonucleases active with either ribo- or deoxyribonucleic acids and producing 5'-phosphomonoesters
EC 3.1.16	Exonucleases active with either ribo- or deoxyribonucleic acids and producing 3'-phosphomonoesters
EC 3.1.21	Endodeoxyribonucleases producing 5'-phosphomonoesters
EC 3.1.22	Endodeoxyribonucleases producing 3'-phosphomonoesters
EC 3.1.25	Site-specific endodeoxyribonucleases specific for altered bases
EC 3.1.26	Endoribonucleases producing 5'-phosphomonoesters
EC 3.1.27	Endoribonucleases producing 3'-phosphomonoesters
EC 3.1.30	Endoribonucleases active with either ribo- or deoxyribonucleic acids and producing 5'-phosphomonoesters
EC 3.1.31	Endoribonucleases active with either ribo- or deoxyribonucleic acids and producing 3'-phosphomonoesters

http://www.chem.qmul.ac.uk/iubmb/enzyme/EC3/cont3aa.html

Substitution of one ester hydrolase for another ester hydrolase would not be expected to produce similar results because of inherent differences in specificity.

Therefore one of ordinary skill in the art would not have had a reasonable expectation of success in substituting one hydrolase for another, even when using hydrolases within the same group.

Two of the inventors in the instant application have described elsewhere, in published application US 2004/0015187 dated June 17, 2004 (a continuation of PCT/FR01/03551, which was published as WO 02/38122 A2 on May 16, 2002), that several enzymes from the same family (that is, able to break the same kind of bond) show different activity according to the tested substrate. See in particular Table 1 with different glycanases and Table 2 with different cellulases. This proves that different enzymes from the same family have different activity. US 2004/0115187 also shows that only some glycosidases (N-glycanase) show activity on *stratum corneum* desquamation whereas similar enzymes (exoglycosidases, especially O-glycanase) have no activity on desquamation. This shows that one cannot expect desquamating activity of an enzyme from the known activity of an enzyme from the same or a close family and directly contradicts the sweeping generalizations of the Fein document. Therefore there is not a reasonable expectation of success in simply substituting one hydrolase for another.

To establish a *prima facie* case of obviousness, the prior art reference must teach or suggest all the claim limitations. Fein does not teach or suggest use of aspartylglucosaminidase, as required by the claims of the instant application. Fein teaches the use of trypsin or trypsin plus papain and generically discloses the use of over approximately different types of 100 hydrolases in EC groups 3.1-3.4 in paragraph [0044] of his specification. Baumann discloses methods of isolating and characterizing human hepatic aspartylglucosaminidase. Baumann does not disclose

the use of aspartylglucosaminidase in promoting desquamation of the skin and/or for promoting hydration of the skin of an individual in need of such treatment. Therefore, the prior art reference does not teach or suggest all the claim limitations.

Furthermore, it is applicants who have discovered and shown in their application that aspartylglucosaminidase (AGA) is present in the epidermis in the *stratum corneum* and has a prodesquamating activity. It is this discovery which has led to the presently claimed methods. Neither Fein nor Baumann et al. suggest that AGA is found in the *stratum corneum* and plays a role in desquamating the skin. No one prior to applicants found AGA in the *stratum corneum* or found it to have a desquamating action therein, which are the findings which led to the present invention. Absent this knowledge, the claims of the current invention would not have been obvious over Fein alone and over Fein in view of Baumann et al.

In view of the foregoing, it is submitted that the claims now in this application are patentable over Fein alone and over Fein in view of Baumann et al.

CONCLUSION

In light of the foregoing, it is believed that all of the claims now in this application are in allowable form. Further, favorable action in the form of a Notice of Allowance are believed to be next in order and are earnestly solicited.

Respectfully submitted,

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